

Fig. 1

# 3D structure topology

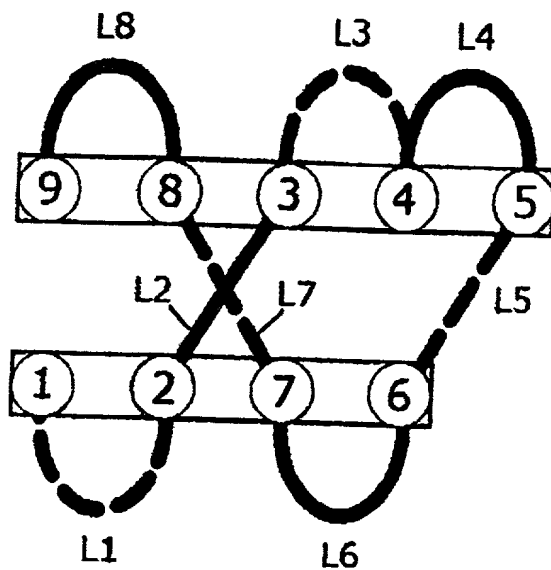
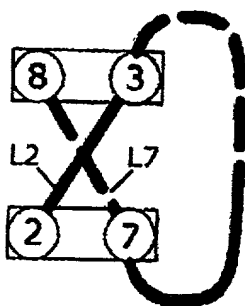


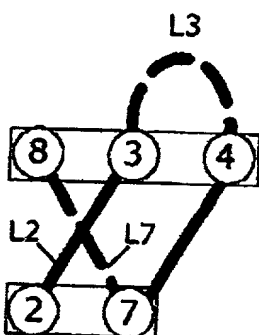
Fig. 2

# Structural Deviations

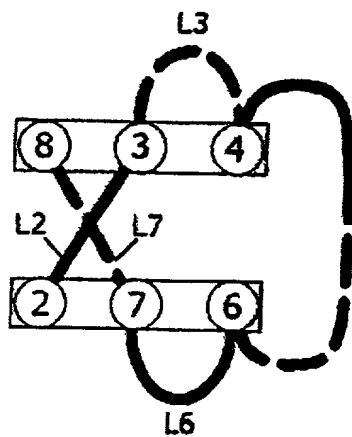
4 beta elements:



5 beta elements:

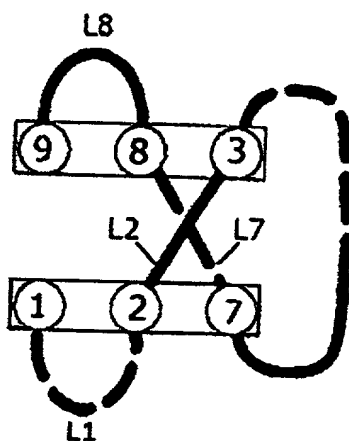


6 beta elements-a:



1GOY: Interleukin-1  
 receptor type 1

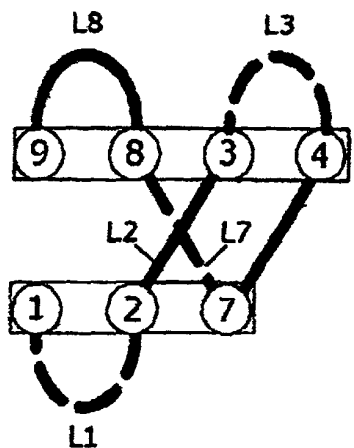
6 beta elements-b:



1J88: Fc epsilon receptor  
 type alpha

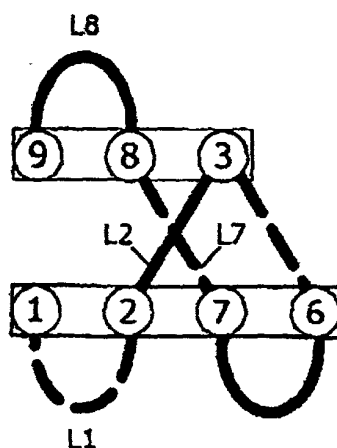
Fig. 3a

7 beta elements-a:



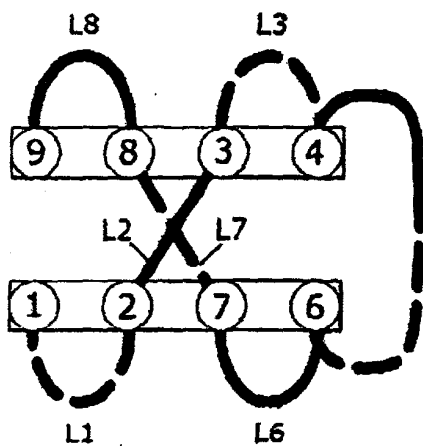
2DL1: Immunoglobulin killer  
 receptor 2dl2

7 beta elements-b:



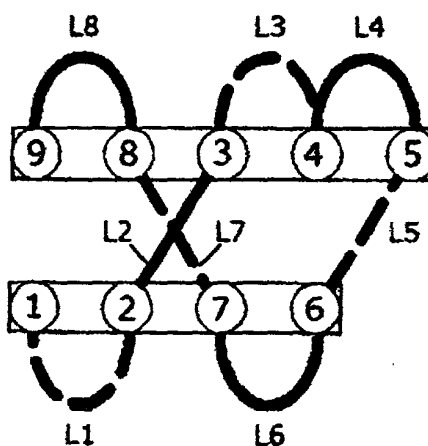
1FF5: E-cadherin domain

8 beta elements:



1IAR: Interleukin-4 alpha receptor

9 beta elements:



All antibody and T-cell receptor  
 variable domains

Fig. 3b

## Modular Affinity & Scaffold Transfer (MAST) Te

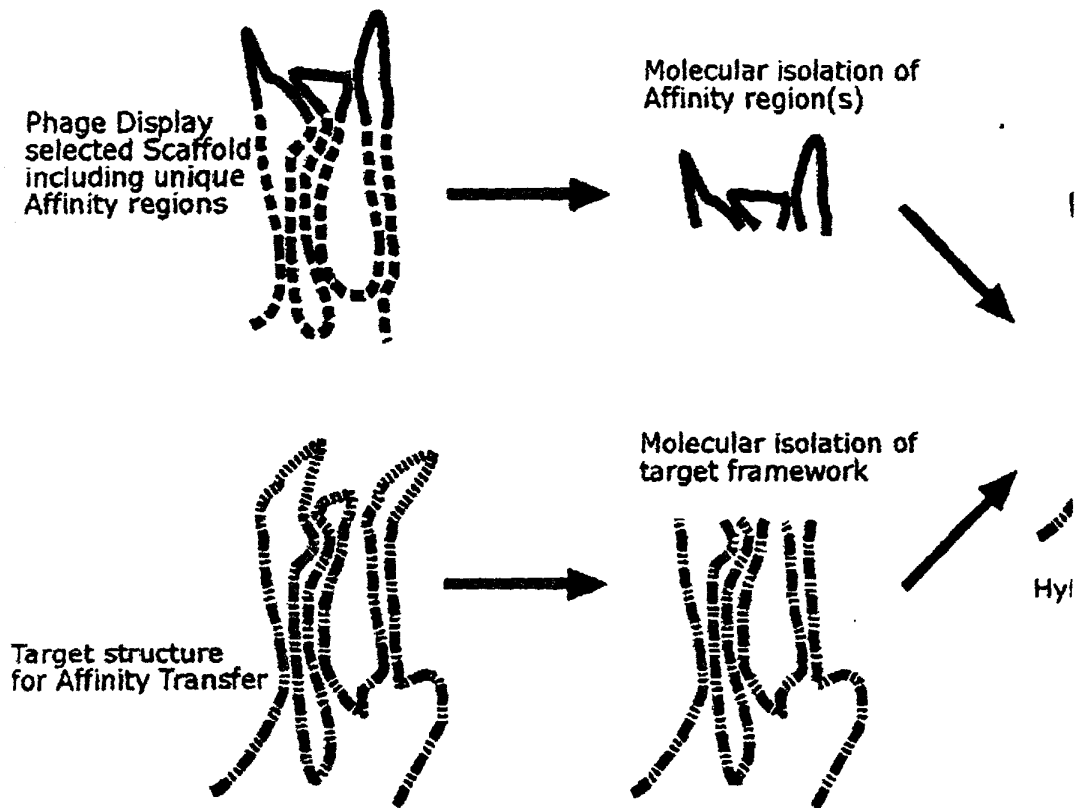


Fig. 4

# STRUCTURAL ALIGNMENT: EXAMPLES OF 1F2X V<sub>H</sub> CAMELID ANTIBODY VARIABLE FRAGMENT

	1	2	3	4	5	6	7	8	9
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1QD0	QVQLQOE-SG--G-GLVQAGGSLRLSCAASGYS	---ASGHGHTGNGWFHQ--VPCK--BREFVAARWAG--	KETWYKOSVKGRTTISODNAKNTVYLOMNSL-K-CE	DTAIYYCAAPVAVADIS---LPVGRDYMGCGTO-VTVS					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
8FAB	AVKLIVQ-AG--G-GVQVQAGGSLRLSCAASGYS	---ISWYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1VSC	-FKTET-TPesR-YLAQIGSVSLTCTGCE	---SPEFSIRVQ-ID--	SPINCKAVTMEG--TTSTILTMNEV-S-PGNEHSY	CTATICE---SKLEK-GIQ-VELY					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1N3	EGSFLA-TC--V--	---NGVCEVTVHG--	AGSKTLAPG-K--	GPITQ--					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1F97	KGSVYT-AGS-G-VQVPEKSLRLSCAASGYS	---SPRVCKEY-Q-GS--TTALVCYMS--	QITAPYADRVTFSS--	SGITFSSV-I-RKDNCEVTCMVSEEGGQ--					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1ENF	VPPTD-LR--IHLIGP--DTMRVTNAPPS	---IDLTFELVRSYKNE--EDVRELSIS--	ISPLIHYTLQEN--SFTPAWDAYEAV--	ISPTOSSTFVVGUS--PWANTTFRVIAENK--					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1CEB	QVAPKLTGI-I-CQAD--RAELHNEQCGDN--	---ISPLIHYTLQEN--SFTPAWDAYEAV--	ISPTOSSTFVVGUS--PWANTTFRVIAENK--	IGASPPSAHSDSCTTG--					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1IAR	IEQNL-TVNT--	---NVSDTLLITWSNFPYPPDNYLYNHLTYAVNISE--	NPPA--DEFRIYVY--	IEPSLRIRAS-CLKSGI-STRAVRPMAQAYN--					
1F2X	QVQLVLE-SG--G-GSVQAGGSLRLSCAASGYS	---VSTYCMGFHQ--APGK--EREQVATIL--G--G	STTIGOSVKGRTTISODNAKNTVYLOMNSL-K-PEDT	AIYYCAGSTVASTGWCSSLIPYDVHYRGQGTO-VTVS					
1F4H	IEQFRI-SG--	---QTIETSEY-IIRHSDNELLHMYVA-LDg--	IFLASGVP--LD--V--	APQKQKLIETPELPQBPESAGQIKLIVRVYQFNATAK--					

## Figure elements explained:

Underlined domains represent (putative) beta-elements 1-9  
Capital letters indicate conserved structural amino acids  
~ indicate the absence of amino acid residues

## Aligned protein domains from:

- 1F2X Single domain camelid antibody Cab-Ca05
- 1QD0 Camelid heavy chain variable domain
- 8FAB Heavy chain from human Iggl
- 1VSC Human Vcam-1
- 1NS3 Structure Of Hcv Protease (Bk Strain) from hepatitis C-virus
- 1F97 Soluble Part Of The Junction Adhesion Molecule From Mouse
- 1ENF Fragment Of Human Fibronectin Encompassing Type-Iii Repeats 7 Through 10
- 1CFB Drosophila neuroglian
- 1IAR Human Interleukin-4 receptor alpha chain complex
- 1F4H E. Coli (Lacz) Beta-Galactosidase (Orthorhombic)

Fig. 5

**Scaffold with V<sub>HH</sub> 1MEL CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A E G Y T I G P Y C M G W F R Q A  
ACGTGCCGTGCTGAAGGTTACACCATTGGCCCGTACTGCATGGGTTGGTTCCGTCAGGCG  
P N D D S T N V A T I N M G G G I T Y Y  
CCGAACGACGACGACTACTAACGTGGCCACGATCAACATGGGTGGCGGTATTACGTACTAC  
G D S V K E R F D I R R D N A S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAACGCTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A G D S  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGATTCT  
T I Y A S Y Y E C G H G L S T G G Y G Y  
ACCATTTACGCGAGCTATTATGAATGTGGTCATGGCCTGAGTACCGGCGGTACCGGCTAC  
D S H Y R G Q G T D V T V S S  
GATAGCCACTACCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

**Scaffold with V<sub>HH</sub> 1BZQ CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A S G Y A Y T Y I Y M G W F R Q A  
ACGTGCCGTGCTAGCGGTTACGCCTACACGTATATCTACATGGGTTGGTTCCGTCAGGCG  
P N D D S T N V A T I D S G G G G T L Y  
CCGAACGACGACGACTACTAACGTGGCCACCATCGACTCGGGTGGCGGGGTACCGTGTAC  
G D S V K E R F D I R R D K G S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAAGGCTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A A G G  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGCGGGTGGC  
Y E L R D R T Y G Q R G Q G T D V T V S  
TACGAACCTGCGCGACCGCACCTACGGTCAGCGTGGTCAGGGTACCGACGTTACCGTCTCG  
S  
TCG

**Scaffold with V<sub>HH</sub> 1HCV CDR regions**

N V K L V E K G G N F V E N D D D L K L  
AATGTGAAACTGGTTGAAAAAGGTGGCAATTCGTCGAAAACGATGACGATCTTAAGCTC  
T C R A E G R T G S T Y D M G W F R Q A  
ACGTGCCGTGCTGAAGGTCGTACGGGTTCCGACCTACGATATGGGTTGGTTCCGTCAGGCG  
P N D D S T N V A T I N W D S A R T Y Y  
CCGAACGACGACGACTACTAACGTGGCCACGATCAACTGGGATAGCGCCGTCGACTACTAC  
G D S V K E R F D I R R D N A S N T V T  
GGTGACTCCGTCAAAGAGCGCTTCGATATCCGTCGCGACAATGCCTCCAACACCGTTACC  
L S M D D L Q P E D S A E Y N C A G G E  
TTATCGATGGACGATCTGCAACCGGAAGACTCTGCAGAATACAATTGTGCAGGTGGTGAA  
G G T W D S R G Q G T D V T V S S  
GGCGGCACCTGGGATAGCCGTGGTCAGGGTACCGACGTTACCGTCTCGTCG

Underlined regions indicate specific affinity regions.

The sequence of underlined regions in each panel represent respectively loop L2 (~CDR1 and AR1), L4 (~CDR2 and AR2) and L8 (~CDR3 and AR4).

Fig. 6a

### Structural topology of a primary scaffold

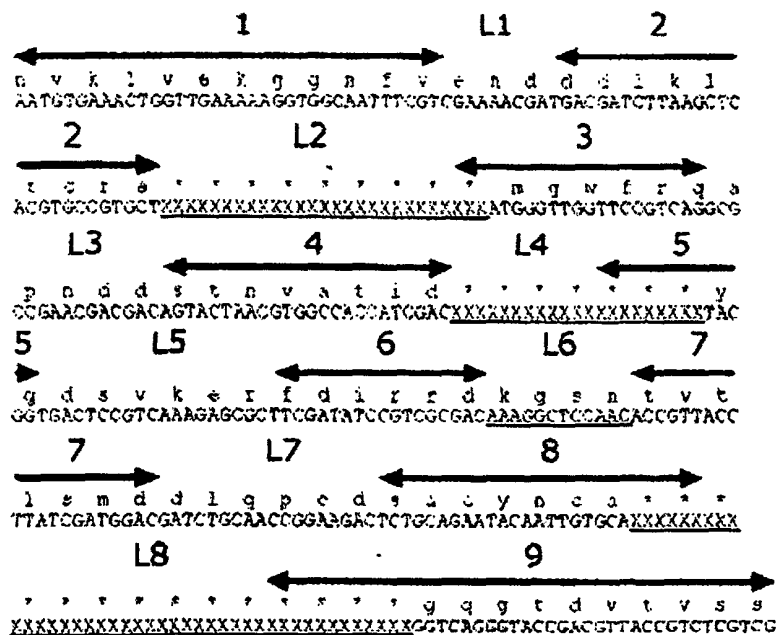


Fig. 6b